SEQ ID No. 6), Factor 7 (Fac7, SEQ ID No. 7) and Tissue plasmiogen activator (Tpa, SEQ ID No. 8). The asterisks indicate conserved amino acids of catalytic triad.--

Please replace the paragraph beginnin on page 10, line 4, with the following rewritten paragraph:

--**Figures 2A-2D** show the nucleotide sequence of the TADG-15 cDNA and the derived amino acid sequence of the TADG-15 protein. The putative start codon is located at nucleotides 23-25. The potential transmembrane sequence is underlined. Possible N-linked glycosylation sites are indicated by a broken line. The asterisks indicate conserved cysteine residues of CUB domain. The SDE-motifs of the LDL receptor ligand binding repeat-like domain are boxed. The arrow shows the arginine-valine bond cleaved upon activation. The conserved amino acids of the catalytic triad; histidine, aspartic acid and serine residues are circled.--

Please replace the paragraph beginning on page 12, line 19, with the following rewritten paragraph:

--**Figures 11A** and **11B** show and alignment of the human TADG15 protein sequence with that of mouse epithin which

demonstrates that the proteins are 84% similar and 81% identical over 843 amino acids. Residues that are identical between the two proteins are indicated by a "-", while he "*" symbol represents the TADG15 translation termination. The most significant difference between these two proteins lies in the carboxy-termini, which for epithin, includes 47 amino acids that are not present in TADG15.

Please replace the paragraph beginning on page 13, line 6, with the following rewritten paragraph:

--**Figures 12A-12E** show a nucleotide sequence comparison between TADG-15 and human SNC-19 (GeneBank Accession No. #U20428).--

Please replace the paragraph beginning on page 33, line 19, with the following rewritten paragraph:

--The invention includes a substantially pure DNA encoding a TADG-15 protein, a DNA strand which will hybridize at high stringency to a probe containing a sequence of at least 15 consecutive nucleotides of (SEQ ID No. 1). The protein encoded by the DNA of this invention may share at least 80% sequence identity (preferably 85%, more preferably 90%, and most preferably 95%) with the amino acids listed in Figures 3

and 4 (SEQ ID No. 2). More preferably, the DNA includes the coding sequence of the nucleotides of Figures 2A-2D (SEQ ID No. 1), or a degenerate variant of such a sequence. This invention also includes a substantially pure DNA containing a sequence of at least 15 consecutive nucleotides (preferably 20, more preferably 30, even more preferably 50, and most preferably all) of the region from nucleotides 1 to 3147 of the nucleotides shown in Figures 2A-2D (SEQ ID No. 1).

Please replace the paragraph beginning on page 34, line 12, with the following rewritten paragraph:

--By "substantially pure DNA" is meant DNA that is not part of a milieu in which the DNA naturally occurs, by virtue of separation (partial or total purification) of some or all of the molecules of that milieu, or by virtue of alteration of sequences that flank the claimed DNA. The term therefore includes, for example, a recombinant DNA which is incorporated into a vector, into an autonomously replicating plasmid or virus, or into the genomic DNA of a prokaryote or eukaryote; or which exists as a separate molecule (*e.g.*, a cDNA or a genomic or cDNA fragment produced by polymerase chain reaction (PCR) or restriction endonuclease digestion) independent of other sequences. It also includes a recombinant DNA which is part of a hybrid gene encoding

additional polypeptide sequence, *e.g.*, a fusion protein. Also included is a recombinant DNA which includes a portion of the nucleotides listed in Figures 2A-2D (SEQ ID No. 1) and which encodes an alternative splice variant of TADG-15.--

Please replace the paragraph beginning on page 37, line 18, with the following rewritten paragraph:

--The probe to which the DNA of the invention hybridizes preferably consists of a sequence of at least 20 consecutive nucleotides, more preferably 40 nucleotides, even more preferably 50 nucleotides, and most preferably 100 nucleotides or more (up to 100%) of the coding sequence of the nucleotides listed in Figures 2A-2D (SEQ ID No. 1) or the complement thereof. Such a probe is useful for detecting expression of TADG-15 in a cell by a method including the steps of (a) contacting mRNA obtained from the cell with a labeled TADG-15 hybridization probe; and (b) detecting hybridization of the probe with the mRNA.--

Please replace the paragraph beginning on page 38, line 15, with the following rewritten paragraph:

--The DNA may have at least about 70% sequence identity to the coding sequence of the nucleotides listed in Figures 2A-2D (SEQ ID

No. 1), preferably at least 75% (*e.g.*, at least 80%); and most preferably at least 90%. The identity between two sequences is a direct function of the number of matching or identical positions. When a position in both of the two sequences is occupied by same monomeric subunit *e.g.*, if a given position is occupied by an adenine in each of two DNA molecules. then they are identical at that position. For example, if 7 positions in a sequence 10 nucleotides in length are identical to the corresponding positions in a second 10-nucleotide sequence, then the two sequences have 70% sequence identity. The length of comparison sequences will generally be at least 50 nucleotides, preferably at least 60 nucleotides, more preferably at least 75 nucleotides, and most preferably 100 nucleotides. Sequence identity is typically measured using sequence analysis software (*e.g.*, Sequence Analysis Software Package of the Genetics Computer Group (GCG), University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, WI 53705).

Please replace the paragraph beginning on page 45, line 4, with the following rewritten paragraph:

--Likewise, a standard Northern blot assay can be used to ascertain the relative amounts of TADG-15 mRNA in a cell or tissue obtained from a patient suspected of having cancer, in accordance with

conventional Northern hybridization techniques known to those of ordinary skill in the art. This Northern assay uses a hybridization probe, *e.g.*, radiolabelled TADG-15 cDNA, either containing the full-length, single stranded DNA having a sequence complementary to SEQ ID No. 1 (Figures 2A-2D), or a fragment of that DNA sequence at least 20 (preferably at least 30, more preferably at least 50, and most preferably at least 100 consecutive nucleotides in length). The DNA hybridization probe can be labeled by any of the many different methods know to those skilled in this art.--

Please replace the paragraph beginning on page 59, line 14, with the following rewritten paragraph:

--A computerized search of GenEMBL databases using the FASTA program (Wisconsin Package Version 9.1, GCG, Madison, Wisconsin) for amino acid sequences homologous to the TADG-15 protease domain revealed that homologies with other known human proteases never exceeds 55%. Figures 1A and 1B show the alignment of the protease domain of TADG-15 compared with other human serine proteases. Using the BESTFIT program, available through GCG, the similarities between TADG-15 and trypsin, chymotrypsin, and tissue-type plasminogen activator are 51%, 46% and 52%, respectively.--

Please replace the paragraph beginning on page 60, line 3, with the following rewritten paragraph:

From the sequence derived from the TADG-15 catalytic domain, specific primers were synthesized to amplify a TADG-15-specific probe for library screening. After screening an ovarian carcinoma library, one 1785 bp clone was obtained which included the 3''end of the TADG-15 transcript. Upon further screening using the 5''end of the newly detected clone, two additional clones were identified which provided another 1362 bp of the cDNA, including the 5' end of the TADG-15 transcript. The total length of the sequenced cDNA was approximately 3.15 kb. The total nucleotide sequence obtained includes a Kozak's consensus sequence preceding a single open reading frame encoding a predicted protein of 855 amino acids (Figures 2A-2D).

Please replace the paragraph beginning on page 60, line 15, with the following rewritten paragraph:

The deduced open reading frame encoded by the TADG-15 nucleotide sequence (Figures 2A-2D, 3 and 4) contains several distinct domains as follows: an amino terminal cytoplasmic tail (amino acids (aa) #1-54), a potential transmembrane domain (aa #55-77), an extracellular

membrane domain (aa #78-213), two complement subcomponents Clr/Cls, Uegf, and bone morphogenetic protein 1 (CUB) repeats (aa #214-447), four ligand binding repeats of the low density lipoprotein (LDL) receptor-like domain (aa #453-602) and a serine protease domain (aa #615-855). The TADG-15 protein also contains two potential N-linked glycosylation sites (aa #109 and 302) and a potential proteolytic cleavage site upstream from the protease domain (aa #614) which could release and/or activate the protease at the carboxy end of this protein. In addition, TADG-15 contains an RGD motif (aa #249-251) which is commonly found in proteins involved in cell-cell adhesion.--

Please replace the paragraph beginning on page 68, line 4, with the following rewritten paragraph:

--Recently, a mouse protein named epithin (GenBank Accession No. AF04282) has been described.[14] Epithin is a 902 amino acid protein which contains a similar structure to TADG-15 in that it has a cytoplasmic domain, transmembrane domain, two CUB domains, four LDLR-like domains and a carboxy terminal serine protease domain. TADG-15 and epithin are 84% similar over 843 amino acids, suggesting that the proteins may be orthologous (Figures 11A and 11B). The precise role of epithin remains to be elucidated.--

Please replace the paragraph beginning on page 68, line 12, with the following rewritten paragraph:

--A search of GeneBank for similar previously identified sequences yielded one such sequence with relatively high homology to a portion of TADG-15 from nucleotide #182 to 3139 and SNC-19 GeneBank Accession No. #U20428) is approximately 97% (Figures 12A-12E). There are however significant differences between SNC-19 and TADG-15. For example, TADG-15 has an open reading frame of 855 amino acids whereas the longest open reading frame of SNC-19 is 173 amino acids. Additionally, SNC-19 does not include a proper start site for the initiation of translation, nor does it include the amino terminal portion of the protein encoded by TADG-15. Moreover, SNC-19 does not include an open reading frame for a functional serine protease because the His, Asp and Ser residues of the catalytic triad that are necessary for function are encoded in different reading frames.--

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IN THE CLAIMS:

Please amend claim 22 as follows:

22. (thrice amended) A kit for detecting Tumor Antigen Derived Gene-15 (TADG-15) protein, comprising:

F15